Medical Information

Refer to: Richardson RG, Parker RG: Metastases from undetected primary cancers—Clinical experience at a radiation oncology center (Medical Information). West J Med 123:337-339, Oct 1975

Metastases from Undetected Primary Cancers

Clinical Experience at a Radiation Oncology Center

R. GARRATT RICHARDSON, MD
ROBERT G. PARKER, MD
Seattle

MANAGEMENT OF PATIENTS with initial symptoms or signs produced by metastases may be difficult but rewarding. The clinical entity in which the presenting findings are related to the distant spread of cancer has been termed "precocious metastasis."[1] There is a subgroup of these patients in whom, despite thorough investigation, no primary tumor site can be identified. These patients often are referred for radiation therapy of their symptomatic metastases. The natural history of a group of these patients has been reviewed.

Materials and Methods

Between 1960 and 1973, 86 patients were referred to the Division of Radiation Oncology at the University of Washington with the diagnosis of metastatic cancer of unknown origin. This was a highly selected group of patients, in that only those patients thought to have metastatic disease which could be palliated by radiation therapy were referred. Thus, patients with liver and lung metastases generally were excluded. The primary site had not been established by the usual investigative procedures. Although most of these patients were older than 50 years, 10 percent were under the age of 40 (Figure 1). There were 63 males and 23 females. Eighty patients were white, three were black and one each was of Chinese, Hawaiian and North American Indian origin.

Bone was the most frequent metastatic site (38 percent) followed by nodes above the clavicle (28 percent), soft tissue (13 percent), brain (13 percent), mediastinum, infraclavicular nodes and lung (Table 1). Examples of soft tissue sites were pelvis, flank, leg, back of neck, umbilicus, buttock, orbit and scalp. The lung lesion was considered metastatic because of an elevated level of serum chorionic gonadotropin.

The biopsy specimens of all the lesions were reviewed by pathologists in the University of Washington teaching hospitals. In seven patients, there was not a histopathologic diagnosis before therapy. In two of these patients, cancer was confirmed at autopsy.

The distribution of histopathologic types in the metastases was undifferentiated malignant tumor —44 patients; adenocarcinoma—23 patients;

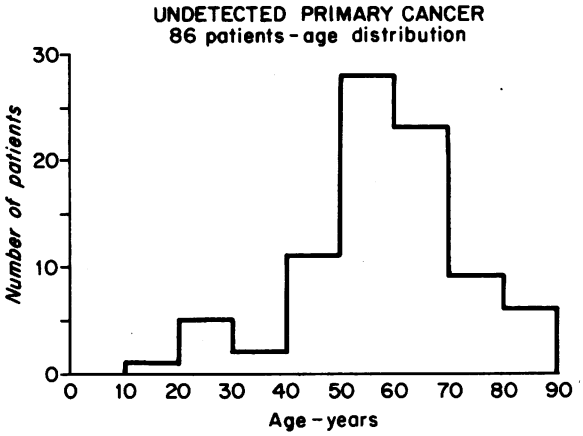

Figure 1.—Age distribution of 86 patients with undetected primary cancer.

TABLE 1.—*Sites of Metastases from Undetected Primary Cancer*

	Number	*Percent*
Bone	33	38.0
Lymph nodes		
above cavicle	24	28.0
below clavicle	3	3.5
Soft tissue	11	13.0
Brain	11	13.0
Mediastinum	3	3.5
Lung	1	1.0
TOTAL	86	100.0

Dr. Richardson is currently with the Virginia Mason Medical Center, Section of Radiation Oncology, Seattle.

Reprint requests to: Robert G. Parker, MD, Division of Radiation Oncology, NN146, University Hospital, 1959 NE Pacific Avenue, Seattle, WA 98195.

squamous cell carcinoma—11 patients (Table 2). The large proportion (50 percent) of the malignancies were undifferentiated cancers, reflecting the difficulty in determining the site of origin.

Treatment

Most patients received palliative radiation therapy to their symptomatic metastatic lesions. In a few patients with cervical node metastases, large tissue volumes including possible primary tumor sites, were treated to high doses with curative intent. The management of cancer in cervical lymph nodes in patients with an unknown primary site has been discussed by a number of authors[2-5] and will not be further elaborated upon here. Many patients who received palliative radiation therapy also received chemotherapy.

TABLE 2.—*Histopathology of Metastases from Undetected Primary Cancer in 86 Patients*

	Number of Patients
Adenocarcinoma (23 patients)	
Well differentiated	1
Moderately differentiated	5
Poorly differentiated	5
Differentiation not given	12
Squamous carcinoma (11 patients)	
Well differentiated	1
Moderately differentiated	3
Poorly differentiated	5
Differentiation not given	2
Undifferentiated (44 patients)	
Carcinoma	33
Sarcoma	1
Malignancy	10
Spindle cell malignant tumor	1
No histology	7

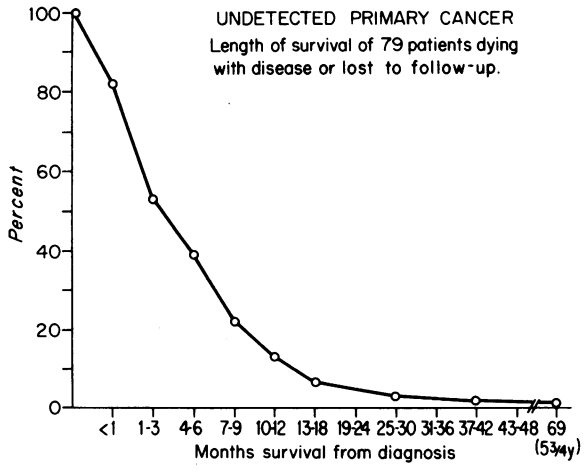

Figure 2.—Length of survival of 79 patients with undetected primary cancer who were dying with disease or lost to follow-up.

Results

In reviewing these data, two subjects were investigated: (1) the prognosis of the patient and (2) the subsequent identification of the primary cancer.

Prognosis

As expected, patients presenting with metastatic disease do not have a good prognosis (Figure 2). The nine patients lost to follow-up have been counted as dead after their last visit. Fifty percent of the patients died within three months of diagnosis and by one year only 12 percent of the patients remained alive: All patients who died had uncontrolled cancer. Some patients with undifferentiated cancers survived from two to five years, receiving additional palliative radiation therapy and chemotherapy. Seven patients were alive at the end of the study, having survived 7, 8, 9, 12, 24 and two for 46 months. Two of these patients had detectable tumor at 8 and 12 months while the other five patients had no evidence of

TABLE 3.—*Histology of Metastasis—Primary Site Subsequently Identified (22 Patients)*

Metastatic Site	*Primary Site*
Adenocarcinoma	
Ilium	Lung
Lumbar spine	Lung
Mediastinum	Lung
Thoracic spine	Prostate
Thoracic spine	Stomach (cytology)
Thoracic spine	Liver
Femur	Thyroid or lung
Squamous Cell Carcinoma	
Rt. supraclavicle	Lung
Mediastinum	Lung
Left neck	Lung
Right neck	Epidermal cyst of neck
Undifferentiated/Poorly Differentiated Malignant Tumors	
Thoracic spine	Lung
Thoracic spine	Lung
Lung	Lung
Groin soft tissue	Lymphoma
Ilium	Lymphoma
Brain	Lymphoma
Ilium	Kidney
Humerus	Kidney
Spine and pelvis	Pancreas
Soft tissue shoulder	Retroperitoneum
Brain	Hepatoma

TABLE 4.—*Metastases from Undetected Primary Cancers—Review of Literature*

Metastatic Presentation	Primary Identified/Number of Patients				
	38/233 ① Cervical Lymph Nodes	214/1,000 ② Supraclavicle Nodes—Infraclavicle Primary	9/42 ③ Axilla	42/162 ④ Adenocarcinoma 70 Percent with Liver Metastasis	22/86 ⑤ All Sites
Primary site					
Head and neck	11	..	1	..	..
Lung	11	67	1	1	9
Esophagus	2	5	..	..	..
Stomach and colon	4	32	2	10	1
Pancreas	2	9	..	16	1
Breast	1	21	1	2	..
Urinary	..	2	..	2	2
Gynecological	..	12	..	..	..
Prostate	1	37*	..	1	1
Lymphoma	3	..	1	..	3
Miscellaneous	3	8	3	10	5

*Antemortem undetected primary not specified.

①Fitzpatrick and Kotalik (1974)
②Nussbaum (1973)
③Copeland and McBride (1973)
④Moertel et al (1972)
⑤University of Washington

cancer. All long-term survivors presented with cervical adenopathy and were treated as primary cancers of the pharynx.

Subsequent Identification of the Primary Cancer

Autopsy examinations were carried out on 22 patients. In three of these, a primary tumor could not be identified. In three other patients, the primary tumor site was detected before death. Therefore, a correlation of precocious metastases and primary tumor sites can be made in 22 patients (Table 3). The most frequent primary site was lung (nine patients) despite apparently nondiagnostic findings on x-ray studies of the chest.

Data from the literature regarding the ultimate identification of an initially undetected primary cancer have been summarized in Table 4.[5-8]

Discussion

Patients with metastases from undetected primary cancer usually are greeted with limited enthusiasm by physicians. Their care often is cursory and is restricted to the treatment of metastases producing immediate clinical problems. Although extended, costly investigation may result in identification of a primary tumor, such activity usually has been considered futile. This long-standing attitude by physicians needs to be reexamined for several reasons: (1) Cervical node metastases may be associated with a primary head and neck tumor which is curable (for example, carcinoma of the nasopharynx or pharyngeal tongue); (2) Specification of the primary site may lead to better directed chemotherapy or endocrine manipulation (for example, kidney, prostate and the three cases of unsuspected lymphoma); (3) Identification of the primary site may aid in anticipating problems (for example, bowel obstruction from carcinoma of the colon), and (4) Definition of the primary site can help in assessing the prognosis for the patient and family.

REFERENCES

1. Rubin P, Green J: Solitary Metastases. Springfield, IL, Charles C Thomas, Publisher, 1968

2. France CJ, Lucas RJ: The management and prognosis of metastatic neoplasms of the neck with an unknown primary. Am J Surg 106:835-839, 1963

3. MacComb WS: Diagnosis and treatment of metastatic cervical cancerous nodes from an unknown primary site. Am J Surg 124:441-449, 1972

4. Jesse RH, Perez CA, Fletcher GH: Cervical lympth node metastasis: Unknown primary cancer. Cancer 31:854-859, 1973

5. Fitzpatrick PJ, Kotalik JF: Cervical metastasis from an unknown primary tumor. Radiology 110:659-663, 1974

6. Nussbaum M: Carcinoma of prostatic origin, metastatic to cervical nodes. NY State J Med 73:2050-2054, 1973

7. Copeland EM, McBride CM: Axillary metastases from unknown primary sites. Ann Surg 178:25-27, 1973

8. Moertel CG, Reitemeier RJ, Schutt AJ, et al: Treatment of the patient with adenocarcinoma of unknown origin. Cancer 30: 1469-1472, 1972